Coronial findings pertaining to non-opioid and non-benzodiazepine drug-related deaths in Australia

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ABSTRACT

Aim: Utilising Australian coroners' inquest findings, this study investigated characteristics of non-opioid and non-benzodiazepine accidental drug-related deaths, and coroners' recommendations applicable to pharmacists.

Methods: Retrospective thematic analysis of narrative text from Australian coroners' inquest findings, published on the internet between January 2012 to October 2017, pertaining to cases of non-opioid and non-benzodiazepine drug-related deaths.

Results: The findings related to a total of 33 non-opioid and non-benzodiazepine drug-related deaths over 5 years; 18 males (mean ± SD age: 50.3 ± 19.3 years) and 15 females (57.7 ± 22.0 years). A wide range of drugs were implicated in drug-related deaths, with drugs relating to mental health conditions (antidepressants and antipsychotics) found to be the most prevalent and increasing over the 5 years. Single-drug toxicity and mixed-drug toxicity drug-related deaths occurred at a similar rate. A history of mental health illness was common. Coroners' comments pertaining to pharmacists were limited to the requirement to maintain accurate records.

Discussion: The coronial findings further highlight the increasing burden of mental health illness in Australia. A greater appreciation of the role of pharmacists as the independent gatekeeper between prescribers and patients is required by coroners, with many coroners' recommendations directed to other professions being relevant to the pharmacists' role of promoting safe and effective use of medicines.

INTRODUCTION

Accidental drug overdoses are an increasing problem in Australia. Deaths rapidly increased between 2001 and 2015, surpassing the national road toll and reaching almost 1,500 deaths annually.[1] Opioids (e.g. heroin, oxycodone, morphine and codeine), benzodiazepines (e.g. diazepam) and alcohol are the primary drugs involved in an accidental overdose, either as the sole agent or in a mixed-drug combination. Literature emphasises that drug overdoses are commonly caused by a combination of drugs.[1-6] The Penington Institute annual overdose report[1] highlights that benzodiazepines are generally only implicated when mixed with other drugs. Pharmaceutical drugs are a contributing factor in over 80% of overdoses, and are the sole drug implicated in over 40% of deaths in Victoria.[7]

All drug-related deaths in Australia are reported to State and Territory coroners for investigation, with selected historical findings published on the internet. A finding comprises a range of narrative texts establishing the identity, medical history and circumstances surrounding an unexpected death. Coroners' inquest findings are recognised as a valuable tool for informing public health action.[8] Witness, pathologist and treating clinician statements, and coroners' recommendations make them conducive to qualitative analysis. As such, this study used coroners' findings to (i) determine the types of pharmaceutical drugs, other than opioids and benzodiazepines, which are contributing to the rise in drug-related deaths in Australia; (ii) identify potential warning signs that may signify a person is at risk of a drug-related death; and (iii) collate the recommendations applicable to pharmacists that have been made in order to improve patient safety and reduce the likelihood of drug deaths.

METHODS

Selected coroners' inquest findings for each Australian State and Territory are published on respective jurisdictional government justice or court websites. A retrospective review of all publically available Australian coroners' inquest findings published on the internet between January 2012 and October 2017 was undertaken. As the data is publically available, ethical approval for this study was not required.

Where databases provisioned a search capability, the search terms ‘drug’, ‘overdose’, ‘medicine’ and ‘medication’ were used to identify all potential drug-related inquests. Where databases did not have a search functionality or appropriate meta-tagging of findings, each finding was reviewed manually. The cause of death and context of matching keywords was examined for returned findings to determine eligibility.

Cases were excluded on the basis of medication not being implicated, or the implicated drug being defined as a Schedule 5, 6, 7 or 9 poison, a pesticide or an unregistered product purchased over the internet.[9] As our interest was in non-opioid and non-benzodiazepine drug-related deaths, cases were further excluded on the basis of the primary contributing drug(s) being an opioid or benzodiazepine, where the dose could be implicated with disregard to any other class of drug present. Finally, cases were also excluded where all primary contributing drugs were used or obtained illicitly, toxicology or clinician reports did not provide sufficient detail, or whereby drug toxicity was the result of an attempt to preserve life.

Details of each deceased individual were recorded (age, gender, year of death and place of residence; medical history pertaining to mental health and chronic pain; alcohol, illicit or prescription drug addiction; and history of self-harm, including overdoses and suicide attempts). Place of residence was coded using the Pharmacy Accessibility Remoteness Index of Australia (PhARIA).[10]

The name, role (sole drug, primary drug, contributing or additive effects) and reported toxicology levels of each drug were recorded. Drugs were classified by generic name and drug class, and coded with a poison Schedule by cross-referencing the *Poisons Standard 2012* (Cth), Register of Therapeutic Goods (ARTG) reference database, and Australian Medical Handbook.[9,11,12] A toxicology grade was determined by correlating forensic pathologist findings relating to drug levels with drug toxicology monographs published in the Handbook of Forensic Toxicology for Medical Examiners Drugs, and were classified as being ‘ceased’ prior to the event, ‘non-toxic’ or ‘therapeutic’, ‘toxic’, ‘toxic-lethal’, or ‘lethal’.[13] Any reference to reasonable doubt, if not specifically ruled on by the coroner, pertaining to pathology results that may have been skewed due to post-mortem drug redistribution, was recorded. All comments and recommendations pertaining to community or hospital pharmacists were collated.

RESULTS

A total of 1,932 coroner briefs were published on the internet between 2012 and October 2017, with the year of death ranging from 2007-15. Excluding briefs with insufficient information or where drugs were primarily used or acquired illicitly (with the exception of cannabis), obtained via the internet (except S4 or S8 medications), a pesticide, or used in an attempt to preserve life, 100 cases were identified as pharmaceutical drug-related deaths. A further exclusion of cases in which opioids or benzodiazepines were identified as the primary cause of death, or pharmaceuticals which were not registered for human use, resulted in 33 drug-related cases for examination (Figure 1) from 6 States. No relevant cases were found in the Northern Territory (NT), while in the Australian Capital Territory (ACT) cases were excluded for lack of qualitative data.

Among the 33 deceased subjects, there were 18 males (mean ± SD age: 50.3 ± 19.3 years) and 15 females (57.7 ± 22.0 years). The deceased's living arrangements were not mentioned in 14 coroner or witness statements; of the other 19 cases, 5 individuals lived alone. Most places of residence (23 of 28 specified) were within PhARIA category 1. Information pertaining to the deceased having being diagnosed with, or managing, a medical or social condition was often provided in statements by family, witnesses or treating practitioners (n=25; 76%). Generally, there were several co-existing conditions. The most prevalent were anxiety and depression (12 cases; 36%), other mental health disorders (not categorised; 11; 33%), alcohol abuse (7; 21%), use of illicit drugs (6; 18%), previous overdose/suicide attempt or threat thereof (6; 18%), chronic pain (5; 15%), and prescription medication misuse (4; 12%).

A total of 52 unique scheduled pharmaceutical drugs and 4 unscheduled substances with pharmaceutical properties were identified. There were increases in cases associated with antidepressants and antipsychotics over the studied period. Ethanol was found to be the leading implicated drug (n=5), followed by quetiapine (n=3) (Figure 2). Digoxin was found to be the sole contributor on two occasions. Citalopram and paracetamol were found to be the sole implicated drug in a single event, and had an additive or co-primary role, respectively, in a subsequent multi-drug toxicity event. The top 10 drugs were implicated in 48.5% of the coronial findings (n=16). Narrow therapeutic index drugs were attributed to 6 (18.1%)

deaths. These drugs were identified as warfarin (n=2), digoxin (n=2), lithium (n=1) and clozapine (n=1).

When any drug at therapeutic or sub-therapeutic levels that was not implicated by the forensic pathologist was discarded, the frequency of single-drug toxicity drug-related deaths was found to be 51.5% (n=17). Of these, 7 were found to have caused death with drugs at a therapeutic level, and two findings were attributed to an anaphylactic reaction. For the cases of mixed-drug toxicity, 2, 3, 4 and 8 individual drugs were involved in 3, 7, 5 and one case, respectively. Only one of these findings reported all drugs contributing to death to be at a therapeutic level. All drugs had been ceased prior to death in one case.

Pharmacists, with the exception of when submitting evidence as expert opinion, were referenced in 5 findings. The dispensing pharmacist provided a statement of evidence in 4 findings. There was one finding in which the pharmacist was found to have contributed to the cause of death. The pharmacist had identified that the dosage on a prescription for methotrexate appeared to be wrong, with directions to administer the drug daily instead of weekly. Evidence suggested that the pharmacist failed to confirm the dosage with the prescriber, dispensed the drug and labelled the container with "No directions specified please check with prescriber if unsure of usage", and counselled the deceased using the Consumer Medicine Information leaflet.[14] The coroner's comment was made in relation to public health:

> "The cause of the failure was an inexplicably incompetent error by a suitably qualified general practitioner, which error had been identified but not effectively corrected by an apparently competent pharmacist for reasons that cannot now be ascertained."

The Pharmacy Board of Australia provided a statement to the coroner, and their 'Guidelines for dispensing of medicines' were submitted as evidence. The coroner commented:

> "I must confess that prior to hearing the evidence at the inquest and subsequently receiving information from the Pharmacy Board of Australia and from the Pharmaceutical Society of Australia website, I had assumed that pharmacists would consider themselves obliged to comply with the directions of prescribing doctors. I have since been disabused of that misconception."

The circumstances of the death were referred to the Australian Health Practitioner Regulatory Agency for consideration. No other findings made formal recommendations directed at pharmacists or pharmacies. Comments pertaining to pharmacists were limited to the requirement to maintain accurate records of drug interventions.

DISCUSSION

All drug-related deaths in Australia are reported to State and Territory coroners for investigation, with selected historical findings published on the internet. These cases, with their accompanying qualitative information, are a useful resource when following trends in drug-related deaths and devising strategies to lessen the numbers of these deaths.

With an average age over 50 years, the individuals who died as a result of accidental drug-related causes were older than, yet with a similar male gender preponderance to, those represented in intentional and all drug-related deaths in Australia.[1] This study also identified mental health conditions (anxiety, depression or other) as a significant risk factor in drug-related deaths.

The study identified a total of 52 scheduled pharmaceutical drugs and 4 unscheduled substances with pharmaceutical properties across 33 coronial findings. A wide range of drugs were implicated in non-opioid and non-benzodiazepine drug-related deaths, with most drugs only being implicated once or twice. When drug classes were grouped to disease management, the most common drugs contributing to deaths were found to be those treating mental health conditions, with increasing prevalence over the period of data collection.

Literature emphasises that drug overdoses are commonly caused by a combination of drugs.[1-7] This study found the rate of single-drug toxicity (51.5%, n=17) and mixed-drug toxicity (48.5%, n=16) to be similar. In line with previous Australian drug trend analysis,[1,7] ethanol was found to be the most prevalent drug (n=5) contributing to mixed drug-related deaths. Ethanol was always found to be at a non-toxic ('therapeutic') level.

Somewhat surprisingly, pharmacists were only mentioned in 15% of the findings. The references were typically limited to the provision of evidence for their dispensing or hospital

discharge activities, or requirements to maintain accurate records. It was apparent that coroners, in general, may not have a well-developed understanding of the professional role of a pharmacist. If the role of the pharmacist, as quoted by Stephen Marty, then Chair of the Pharmacy Board of Australia: [14]

> "is the independent gatekeeper of safety between subscriber and patient to ensure that the patient receives the right drug in the right dose and frequency, and that the patient understands the information provided to them in order to maximise therapeutic effectiveness and minimise any adverse effects"

was understood by coroners, then we would have expected to see many more recommendations pertaining to the prevention of accidental drug-related deaths, directed to pharmacists. Many of the recommendations made to general practitioners were equally relevant to pharmacists, including the need for increased monitoring when commencing a narrow therapeutic index drug or adding an additional drug. Also, anaphylactic reactions accounted for 6% of deaths, reiterating the requirement to vigilantly enquire about and clearly document patient allergies.

The study has some limitations. Results were limited by accessibility to 'selected' publically available coronial inquest findings. The coroner only reviews sudden and unexpected deaths, and deaths must be reported correctly and in a timely fashion in order to obtain reliable pathology results. Post-mortem redistribution of many drugs can make it difficult to accurately interpret toxicology results.

In conclusion, this study used a qualitative analysis of the narrative text in coroners' findings for accidental drug-related deaths to examine the prevalence and nature of implicated pharmaceutical drugs, risk factors, coroners' recommendations and findings applicable to pharmacists. A range of drugs were implicated in drug-related deaths, when the primary contributing opioid and benzodiazepine drugs identified in other studies were excluded.[1-7] Drugs relating to mental health conditions were found to be the most prevalent. A greater appreciation of the role of pharmacists as the independent gatekeeper between prescribers and patients is required by coroners. Many of the recommendations made to medical practitioners were also relevant to pharmacists when performing safe dispensing practices

and patient counselling, as part of their role of promoting safe and effective use of medicines.

REFERENCES

1. Penington Institute. Australia's Annual Overdose Report 2017, Melbourne: Penington Institute; 2017.

2. Roxburgh A, Ritter A, Slade T, Burns L. Trends in drug use and related harms in Australia: 2001 to 2013. Sydney: National Drug and Alcohol Research Centre, University of New South Wales; 2013. Available from: https://ndarc.med.unsw.edu.au/sites/default/files/ndarc/resources/Australian%20Drug%20Trends%202001%20to%202013.pdf.

3. Monheit B, Pietrzak D, Hocking S. Prescription drug abuse - a timely update. Australian Family Physician. 2016;45(12):862-6.

4. Nicholas R, Lee N, Roche A. Pharmaceutical drug misuse in Australia: complex problems, balanced responses. Adelaide: National Centre for Education and Training on Addiction (NCETA), Flinders University; 2011.

5. National Coronial Information System (NCIS). NCIS fact sheet: opioid related deaths in Australia (2007-2011). Victoria: Victorian Department of Justice; 2014. Available from http://www.ncis.org.au/wp-content/uploads/2014/08/NCIS-Fact-sheet_Opioid-Related-Deaths-in-Australia-2007-2011.pdf

6. Ogeil RP, Heilbronn C, Lloyd B, Lubman DI. Benefits and challenges to the implementation of real-time prescription monitoring. Medicine Today. 2015;16:18-21.

7. Coroners Court of Victoria. Pharmaceutical drugs in fatal overdose: a coroner's perspective. Victoria: Coroners Court of Victoria; 2015. Available from: http://www.coronerscourt.vic.gov.au/resources/b26dd3d9-4aed-4a48-9fc7-cc3503a9a238/coroners+prevention+unit+-+pharmaceutical+drugs+in+fatal+overdose+-+17march2015.pdf.

8. Bugeja L, Clapperton AJ, Killian JJ, Stephan KL, Ozanne-Smith J. Reliability of ICD-10 external cause of death codes in the National Coroners Information System. Health Information Journal. 2010;39(3):16-26.

9. *Poisons Standard October 2017* (Cth). Australian Government. https://www.legislation.gov.au/Details/F2017L01285/Html/Text#_Toc471222309

10. Department of Health. PhARIA values 2017-2018. Adelaide: Hugo Centre for Migration and Population Research; 2017. Available from: https://www.adelaide.edu.au/hugo-centre/spatial_data/pharia/.

11. Therapeutic Goods Administration. Australian register of therapeutic goods. Canberra: Department of Health; 2017. Available from: https://tga-search.clients.funnelback.com/s/search.html?query=&collection=tga-artg.

12. The Royal Australian College of General Practitioners, Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists, Pharmaceutical Society of Australia. Australian Medicines Handbook 2016. Adelaide: Australian Medicines Handbook; 2016.

13. Molina DK. Handbook of forensic toxicology for medical examiners. Boca Raton: Taylor & Francis; 2010. Available from: http://www.crcnetbase.com.ezproxy.canberra.edu.au/isbn/9781420076424.

14. Coroner's Court of Western Australia. Inquest into the Death of Daniel Lahengking. Perth: State Coroner; 2014. Inquest No.: [not stated]. Available from: http://www.coronerscourt.wa.gov.au/_files/Lahenking%20finding.pdf.

Figure 1. Coroners' briefs pertaining to non-opioid and benzodiazepine drug-related deaths, outlining the search method to obtain the dataset for qualitative analysis.

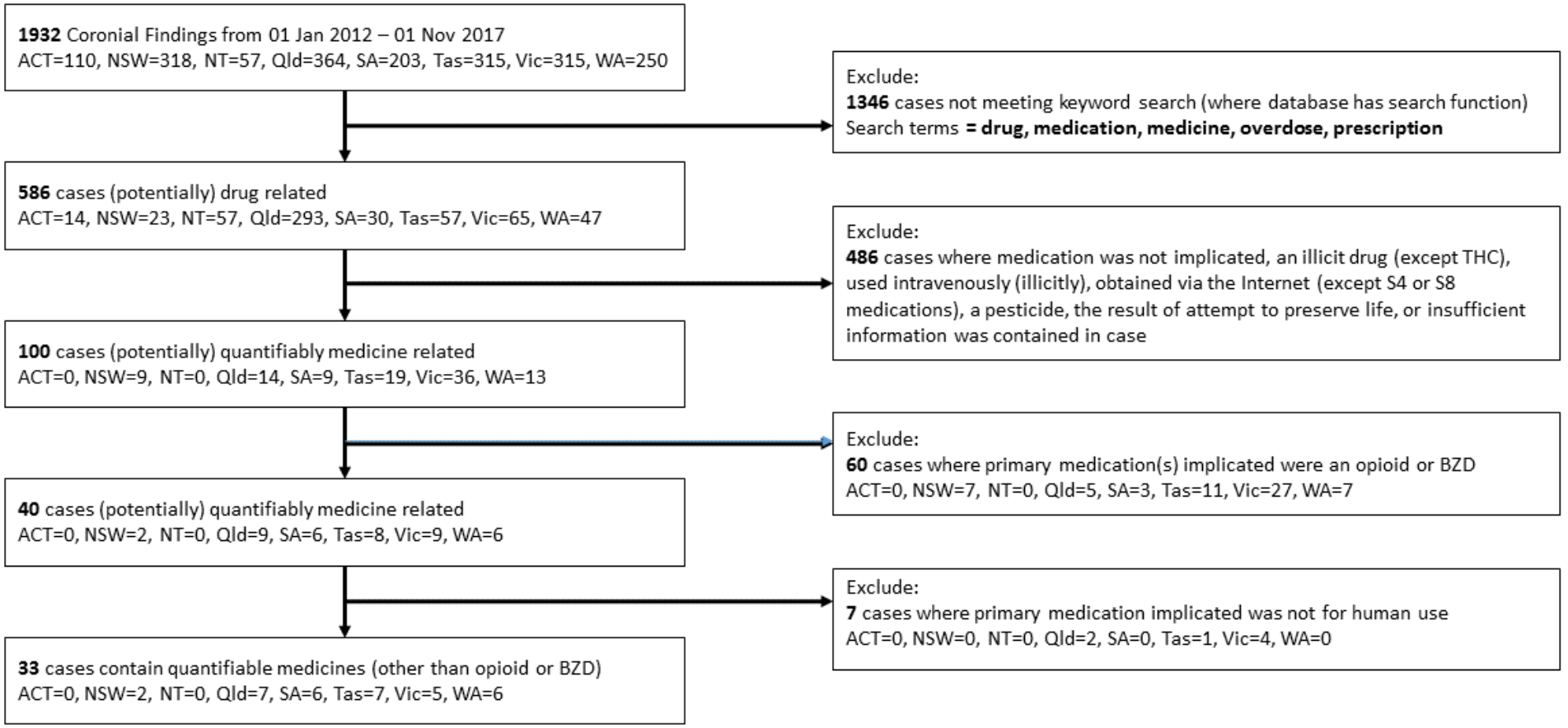

Figure 2. Top 10 drugs implicated in drug-related deaths by role, as a single drug or as part of a multi-drug toxicity event.